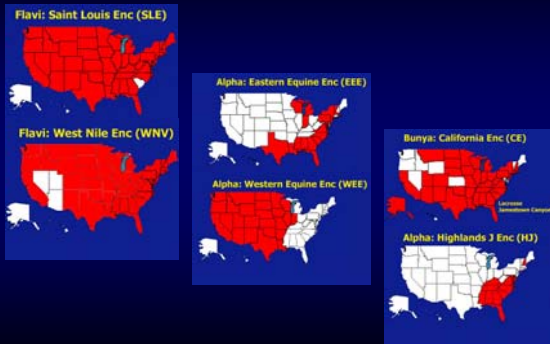


West Nile Neuro Invasive Disease

Infectious Disease Epidemiology Section
Office of Public Health
Louisiana Dept of Health & Hospitals
...Your Taxes at Work...

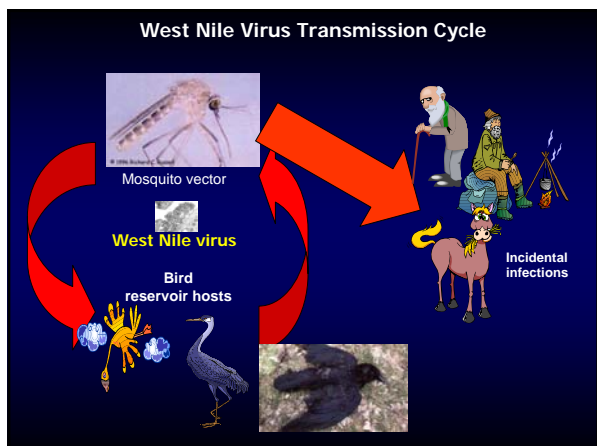
Encephalitis in the USA

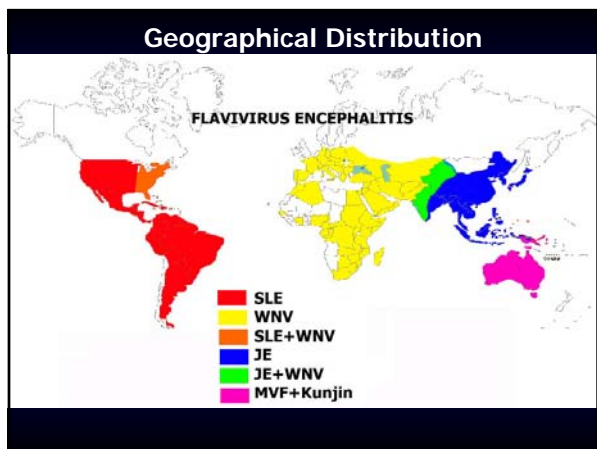


West Nile Virus



- First isolated in 1937 in Uganda (West Nile Province) from blood of a febrile woman
- Family: Flaviviridae (single stranded RNA virus)
 - Genus: Flavivirus
 - Japanese Encephalitis Antigenic Complex
 - Complex includes: Alfuy, Japanese encephalitis, Kokobera, Koutango, Kunjin, Murray Valley encephalitis, **St. Louis encephalitis**, Stratford, Usutu and **West Nile viruses**
- All transmissible by mosquitoes, reservoir in birds
- First recorded epidemic in Israel in 1950's
- Soon recognized as one of the most widespread Flaviviruses
- Distributed through Africa, West Asia, Europe and the Middle East



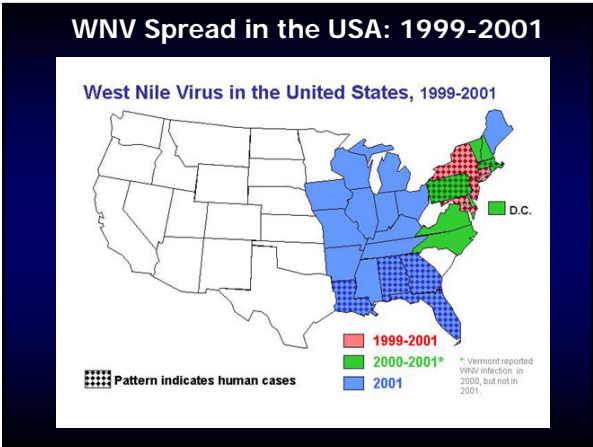


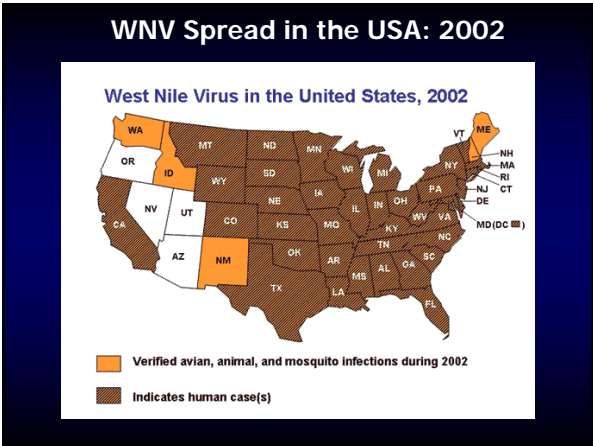
West Nile Outbreaks

- Israel - 1951-1954, 1957(Nursing homes)
- France - 1962
- South Africa - 1974
- Romania – 1996 (393 cases)
- Italy 1998
- Russia - 1999
- United States –1999-2002
- Israel – 2000
- France - 2000

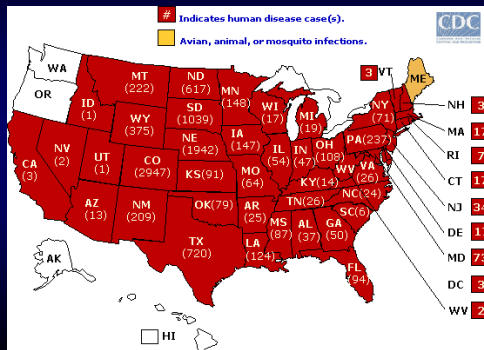
The map shows the locations of West Nile outbreaks in Europe. Black dots are placed on the map to indicate the specific locations where outbreaks occurred.

WNV Spread in the USA						
Year	States	Human	NID	Birds	Mosq Pools	Horses
1999	4	62	62	7	16	25
2000	11	21	21	4,305	515	63
2001	27	66	66	7,332	919	731
2002	39	4,156	2,942	15,745	6,033	12,038
2003	45	9,862	2,866	11,597	7,847	5,145
2004	47	2,470	900	7,331	8,371	1,386
2005	49	2,949	1,272			

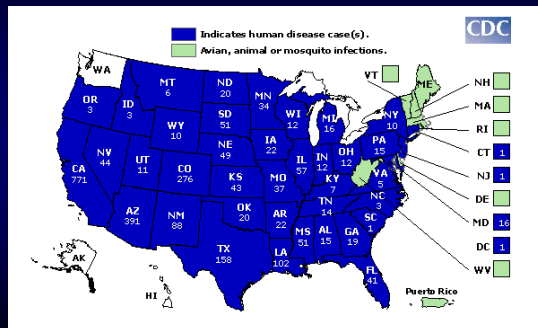




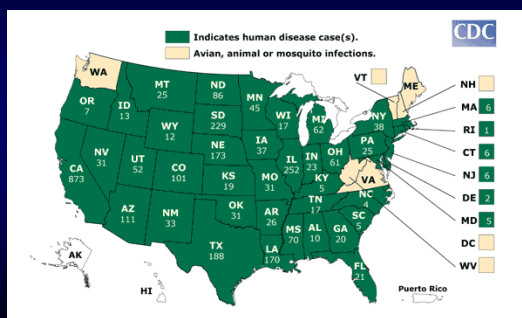
WNV Spread in the USA: 2003



WNV Spread in the USA: 2004



WNV Spread in the USA: 2005



Some Possible Pathways of Introduction

- Infected human host
- Human-transported vertebrate host
 - Legal
 - Illegal
- Human-transported vector(s)
- Storm-transported vertebrate host (bird)
- Intentional introduction (terrorist event)

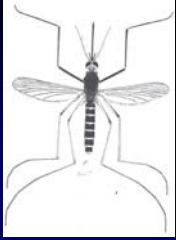



Mosquitoes

West Nile Virus: Entomology



- Isolated from over 40 mosquito species, 29 in the USA
- Only few play a major role in transmission
- Mostly *Culex* species:
 - *Cx. univittatus*, *Cx. pernixguus*, *Cx. pipiens*, *Cx. modestus*, *Cx. quinquefasciatus*, *Cx. tritaeniorhynchus*, and *Cx. Vishnui*
- Other mosquito species in a variety of genera:
 - *Aedes*, *Aedeomyia*, *Anopheles*, *Coquillettidia*, *Mansonia*, *Mimomyia*
 - Other species as accessory vectors?
- Isolated from ticks:
 - Soft tick genera: *Argas*, *Ornithodoros*
 - Hard tick genera: *Amblyomma*, *Dermacentor*, *Hyalomma*, *Rhipicephalus*


Culex quinquefasciatus Southern House Mosquito



Ubiquitous species: abundant in tropical and subtropical countries

Egg Laying: Females lay single raft of 140-340 eggs on heavily polluted small water collection after each blood meal. Eggs hatch in 1-2 days

Egg to Adult: 8-12 days after laying

Breeding place: all types of large man-made containers and collections of ground water, storm sewer catch basin, ground pools, ditches, run off from sewage plants, small artificial containers, cesspits, drains, septic tanks, unused wells, storm water canals



Culex quinquefasciatus Southern House Mosquito


Flying range: up to 3,600 feet /night


Life span: 2 weeks

Biting activity: usually attack humans towards the middle of the night indoors and outdoors; indoor biting


Preferred food: more attracted to birds (poultry) > humans

Vector:
Avian malaria (*Plasmodium relictum*)
Dog heartworm (*Dirofilaria immitis*)
Wuchereria bancrofti in Oriental & Afrotropical
Japanese encephalitis virus in Vietnam






Culex quinquefasciatus




Southern House Mosquito





Aedes albopictus
Asian Tiger Mosquito




Aedes albopictus

Oriental mosquito: recently invaded US (Houston 1985)

Morphology: white bands on legs; medium narrow band on thorax

Breeding place: all types of small peridomestic sites; man-made containers, tin cans, jars, bottles, dishes, wading pools, flower vases, clogged roof gutters, tires + + +

Aedes albopictus
Asian Tiger Mosquito




Flying range: ~500 yards

Biting activity: aggressive, lands & bites immediately, day time

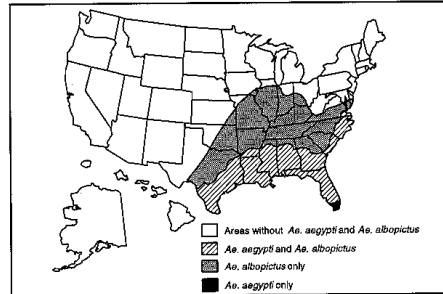
Preferred food: humans

Vector: urban yellow fever, dengue, dog heartworm



Aedes aegypti & *A. albopictus*

FIGURE 1. Distribution of *Aedes aegypti* and *Aedes albopictus* mosquitoes — United States, 1992



Culex salinarius



Louisiana coastal areas mostly

Morphology: Brown species, proboscis and tarsi dark, irregular narrow bands on abdomen

Breeding place: fresh and brackish water in marshes; ponds, pools, ditches, barrels, bilge water from boats, artificial containers around homes

Flying range: 1 mile

Biting activity: mostly outdoors, occasionally indoors; dusk, first hours of darkness

Season: Spring and Fall

Vector: secondary vector of SLE, EEE



Birds & Mammals

Birds

- Isolated from numerous wild birds
- Wetland and terrestrial species
- Birds are primary amplifier hosts
- Migratory bird role in distribution
 - Viremia lasts several days
 - Migratory birds travel far in a few days
- Strain highly infectious for North American birds
- Causing mortality and high viremia

Dead birds
= easy preys for mosquitoes =
role in amplifying virus



Direct transmission from crow to crow in cages
•Virus in urine and feces
•Pecking
•STD???

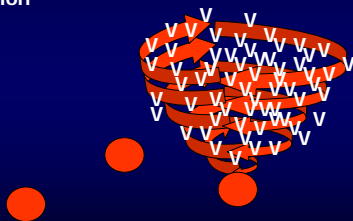
Mammals

- Infected with WN virus
 - Mortality (big brown bat, little brown bat, rabbit, chipmunk, gray squirrel, horse, cat)
 - Seropositive dog
- Valuable as surveillance indicators
 - Identification of species for use as sentinels?
- Role of vertebrates is not known



Why Here and not There?

Viral amplification
occurs in tornado-like
fashion



How Much ?

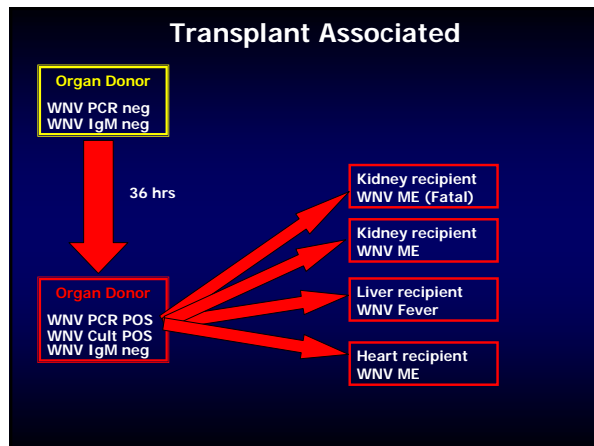
- 100,000 population/4 pop/household = 25,000 household
- *300 quincles /HH /day = 7,500,000 quincles in backyards
- ~10% bites humans = 750,000 bites /night
- 5/1,000 mosquitoes infected = 3,750 infections /night
- 1/200 gets Meningo-encephalitis = 18.75 disease /day /week = 139 disease /week
- Every one is infected in several months, total number of cases =500

Other Modes of Transmission

Transfusion Associated

- 60 investigations, Aug 2002
– Jan 2003
– 20 confirmed cases
– 14 infectious unit donors identified
- Transmitted in RBCs, plasma & platelets
 - Virus isolated from 1 stored plasma unit
 - 5/14 infectious donors were asymptomatic
 - 7/20 confirmed recipients were asymptomatic

- Surveillance of Presumptive Viremic Donors (PVD):
- 84% develop no disease
 - 15% WN Fever
 - 1% NeuroInvasive disease



Transplacental Transmission

- Late 2nd trimester infection
- Prolonged clinical illness in mother
- Child:
 - Chorio-retinitis
 - Bilateral white matter loss in temporal /occipital lobe
 - Temporal lobe cyst
 - Cord and heel: WNV IgM Positive
 - CSF: WNV IgM Positive
 - TORCH, CMV, LCMV Neg
 - HSV, WNV PCR negative

Transmission in Milk

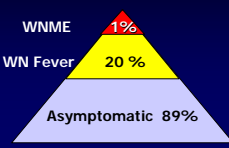
- In 2002: 6 infants < 1
- 1 asymptomatic (breast-feeding associated)
- 5 WNV ME
 - 1 breast-fed BUT mother not infected
 - 4 not breast-fed in month before illness

Clinical & Diagnosis

West Nile: Scope of Human Disease


Incubation period usually 5 to 15 days

- Asymptomatic
- **WEST NILE FEVER (1/10-1/20)**
 - Febrile, influenza-like illness with abrupt onset
 - Moderate to high fever
 - Headache, sore throat, backache, myalgia, arthralgia, fatigue
 - Rash, lymphadenopathy
- **ACUTE ASEPTIC MENINGITIS OR ENCEPHALITIS (1/150-1/300)**
 - CNS involvement and death in minority of cases
 - Severe muscle weakness (50% in NY)
 - Complete Flaccid Paralysis (10% in NY)
 - Axonal and demyelinating syndromes
 - GBS-like
- Most fatal cases >50 years old



WNME 1%
WN Fever 20 %
Asymptomatic 89%

<65 ME = 1/300
65+ ME = 1/50




Mortality and Long Term Sequelae

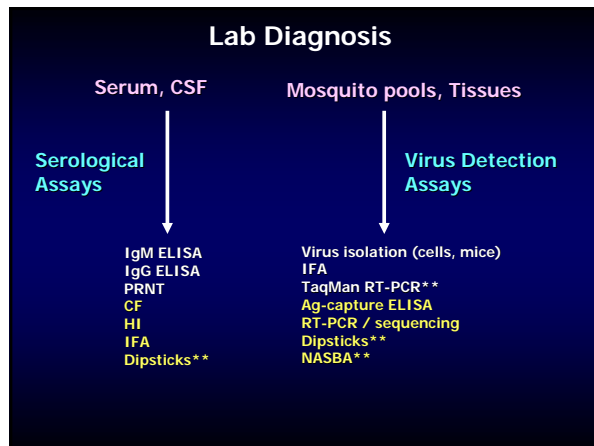
Case fatality rate:

- 4% in Romania/1996
- 12% in NY/1999
- 14% in Israel/2000
- Higher in >70 and hospitalized (up to 25%)

Sequelae: (at 1 year in NY/1999)

Fatigue	67%
Memory loss	50%
Difficulty walking	49%
Muscle weakness	44%
Depression	38%






Louisiana Arbovirus Testing

IFA - Arbo Panel					
Alphavirus		California Virus		Flavivirus	
EEE, WEE		LaCrosse		SLE, WNV	
IgM	IgG	IgM	IgG	IgM	IgG
EIA - PanBio		EIA - CDC			
WNV		WNV		SLE	
IgM		IgM		IgM	

EIA: IgM Antibody Capture Enzyme Linked Immuno Absorbent Assay



The bottom of the tube is coated with an Anti-Human IgM. The serum of the patient is added, then the antigen (extract from WNV), then an anti-WNV antibody tagged with an enzyme, then a substrate that will change color in the presence of the enzyme.

If the serum contains anti-WNV antibodies, the sandwich is complete and the substrate will change color: this is a positive reaction.

If the serum does NOT contain anti-WNV antibodies, one of the layer of the sandwich is missing, the upper layers of the sandwich do not stick. When the substrate is added, there is no change in color. This is a negative reaction.

The optical density of the reaction measures the intensity of the reaction

EIA Controls

For each serum several tests are done:

1-Test with patient serum and WNV antigen. This the "test antigen"

2-Test with patient serum and material on which WNV grew but free of WNV. This is the "normal antigen"

The ratio of patient/test antigen over patient/normal antigen must meet certain criteria to be acceptable.

3-Test with negative control

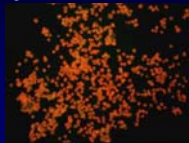
The ratio of patient/test antigen over negative control must meet certain criteria to be acceptable.

These sets of reactions are performed in triplicate and an average of the 3 are done.

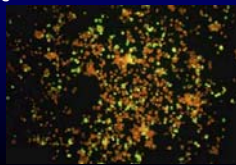
Tests are done with both WNV and SLE antigens. Those with WNV infections have higher results with the WNV antigen than with the SLE antigen.

IFA: Immuno Fluorescence Test

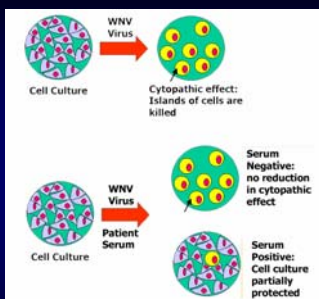
Negative



SLE IgM Pos 1/16 to >1024

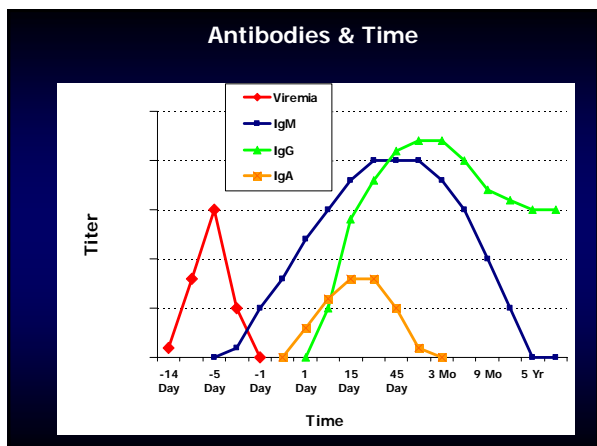


Plaque Reduction Neutralization Test

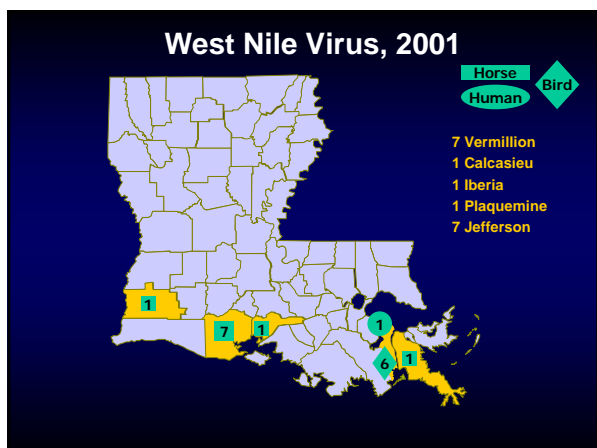


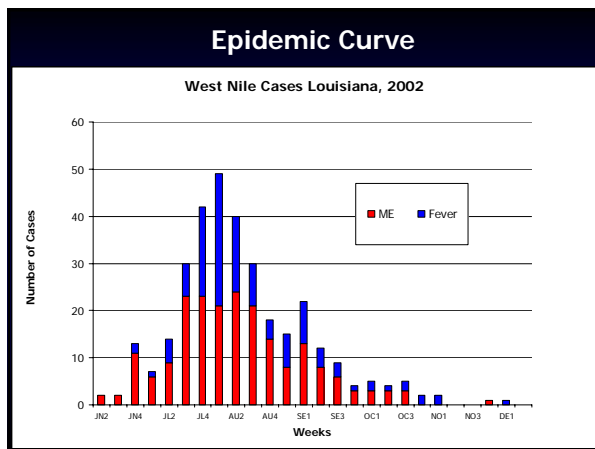
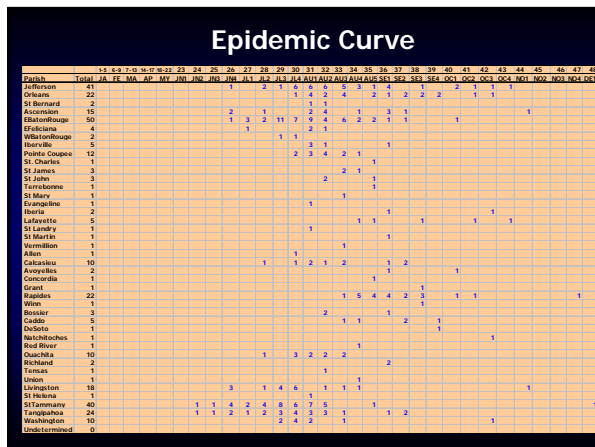
- Tested serum added to live virus and cell culture
- If there are antibodies against the virus in the test serum
 - reduction in virus damage
 - compared to control with no antibodies

- Best test for differentiating WNV from SLE, dengue or Yellow Fever
- BUT
 - It requires handling cell cultures and live virus
 - It takes several days to evaluate plaque reduction

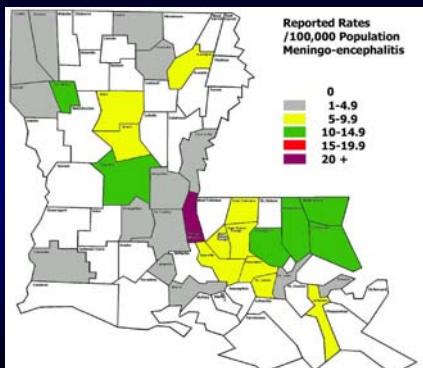


2001 WNV Comes to Louisiana





Meningoencephalitis Reported Rates

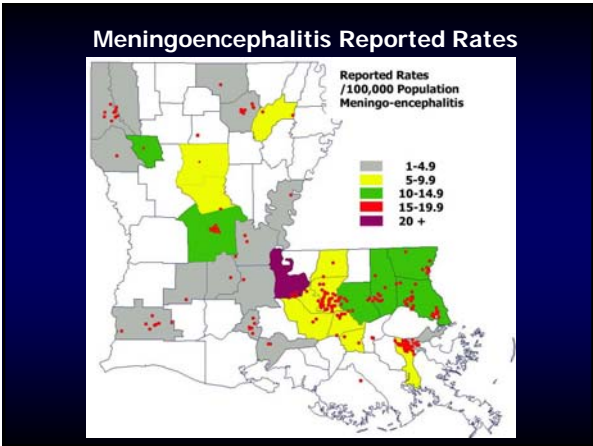


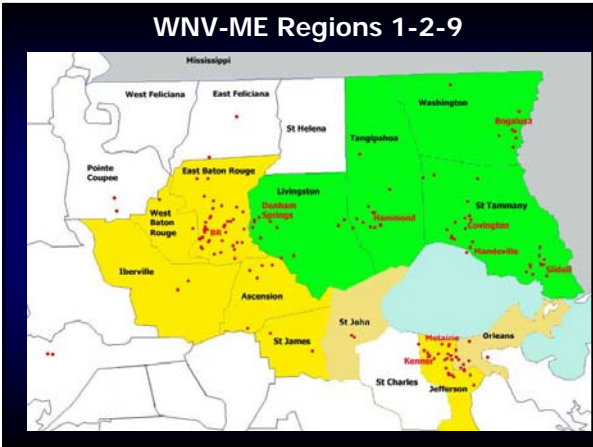
Geographical Distribution of Cases

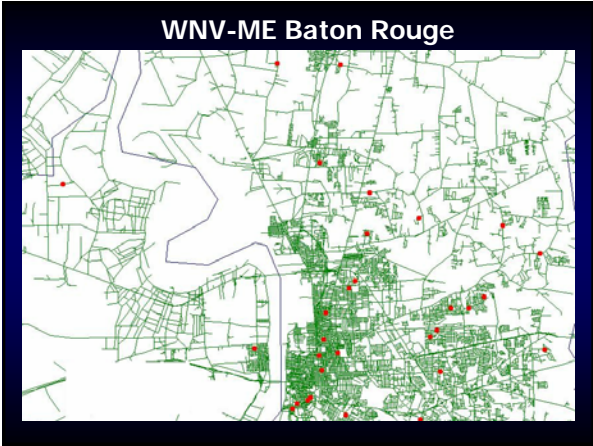


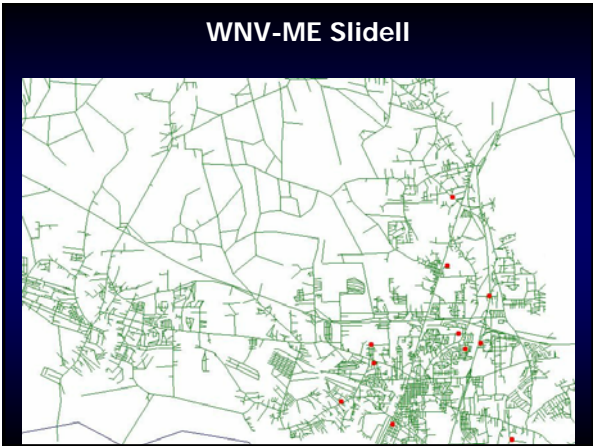
West Nile Neuro-Invasive Disease Louisiana, 2002

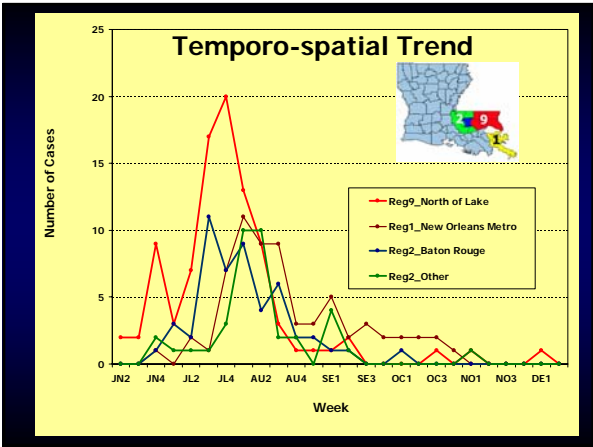


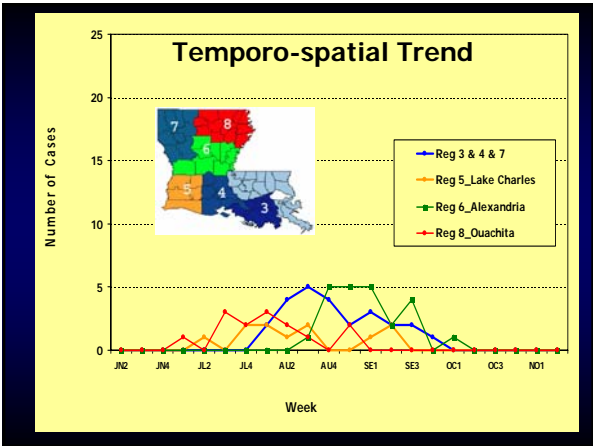


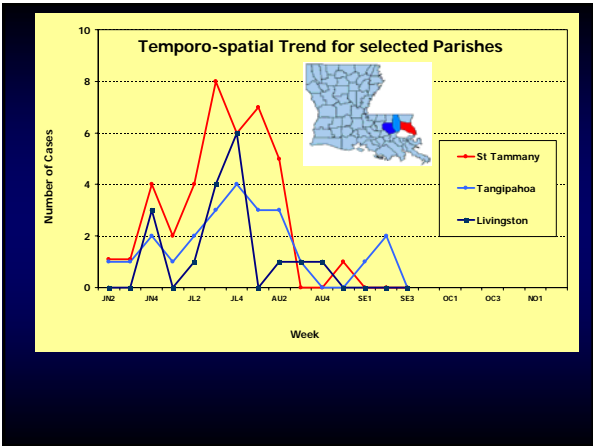


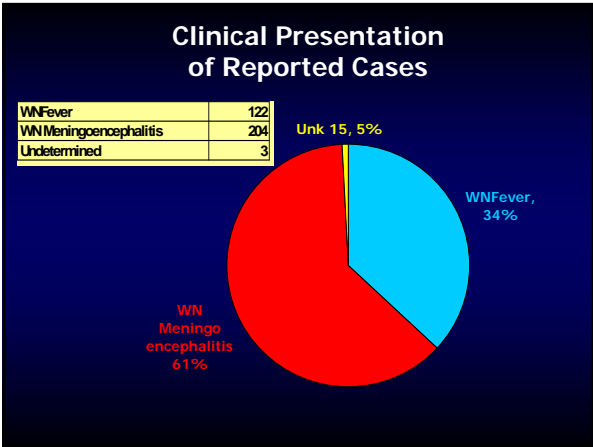


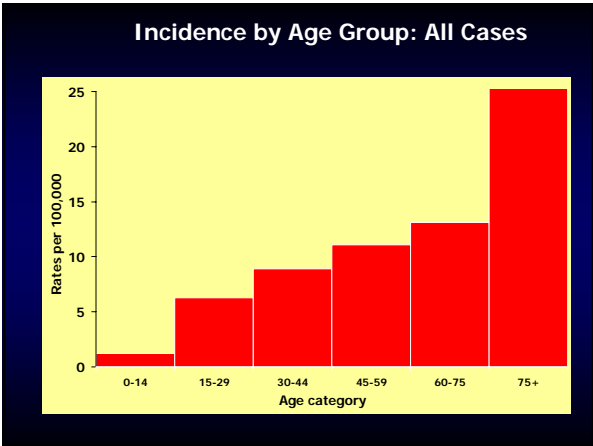


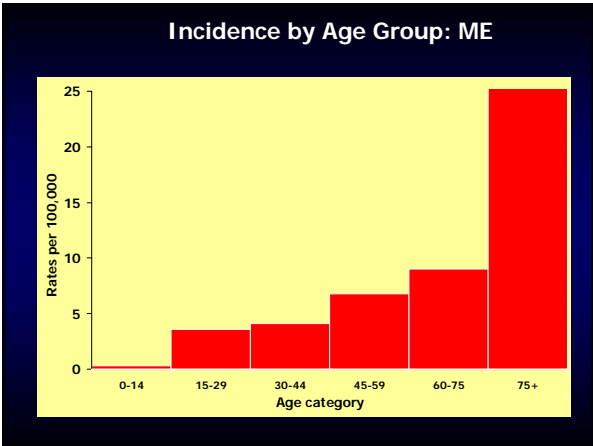


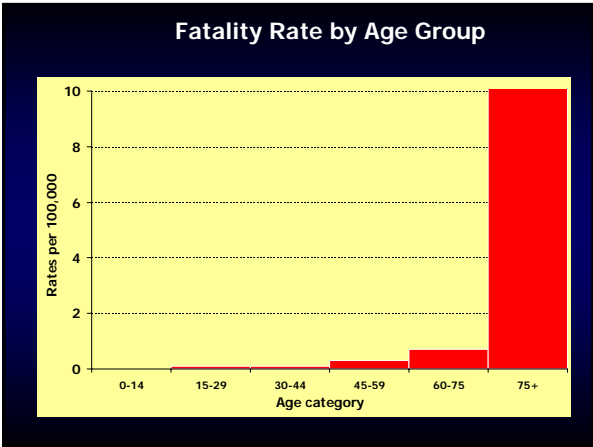


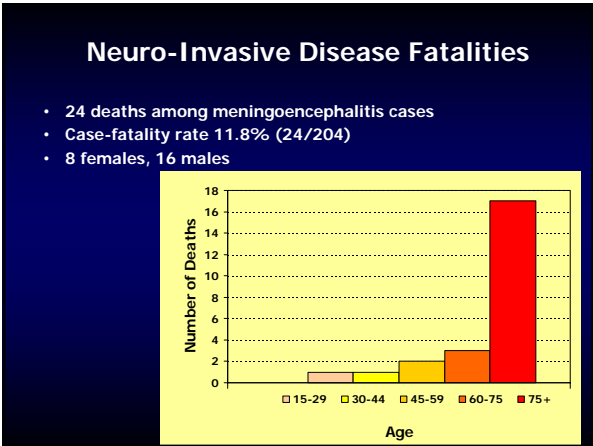






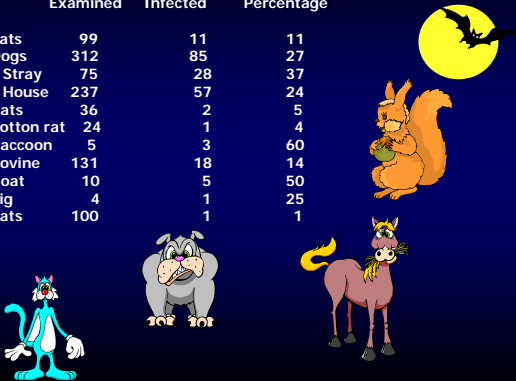






Prevalence Surveys			
Location	# Surveyed	Positives	Prevalence
NYC, Queens, 1999	677	19	2.6
NYC, Staten Is, 2000	871	4	0.5
NY St, Suffolk, 2000	834	1	0.1
CT, Fairfield Co, 2000	731	0	0.0

Mammals in Slidell, La			
	Examined	Infected	Percentage
Cats	99	11	11
Dogs	312	85	27
Stray	75	28	37
House	237	57	24
Rats	36	2	5
Cotton rat	24	1	4
Raccoon	5	3	60
Bovine	131	18	14
Goat	10	5	50
Pig	4	1	25
Bats	100	1	1



2003

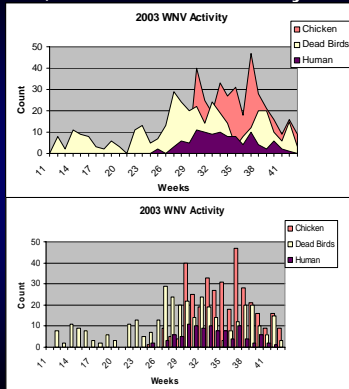
West Nile NeuroInvasive Disease Louisiana, 2003

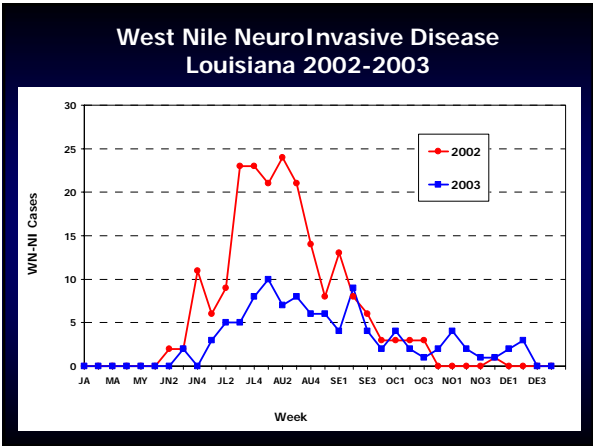


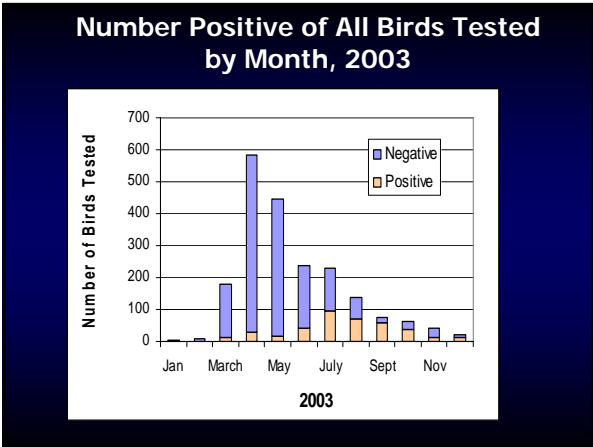
2003 WNV Surveillance

- 15,883 birds were reported by the public
 - 2,059 birds were tested and 390 were WN+
 - 387 Sentinel chickens
 - 201 Mosquito pools
 - 36 Horses
-
- 121 Human cases (101 ME, 20 Fever)
 - 2 infected out of state
 - 8 deaths

Human, Chicken and Bird data by Week







2003 Tested Dead Birds

2003 Tested Dead Birds			
Bird Type	No. Tested	No. Pos.	%Pos.
Crow	109	37	33.9
Blue Jay	607	190	31.3
Other	15	4	26.7
Sparrow	599	81	13.5
Cardinal	483	61	12.6
Grackle	170	14	8.2
Raptor	68	5	7.4
Seagull	4	0	0

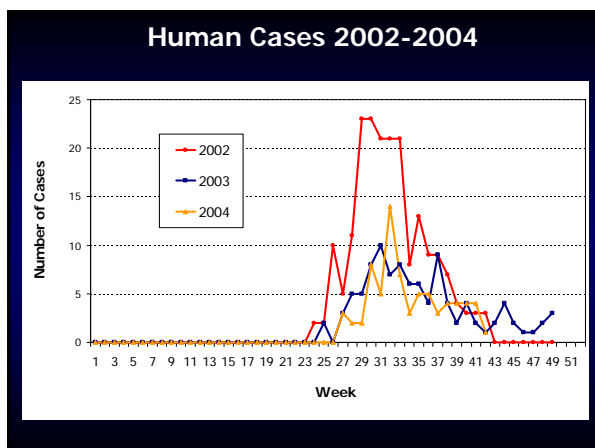


Alligator Farms

- High hatchling mortality at 4 LA farms
- Isolated to 1 building
- Alligators bitten around eyes & mouth
 - Most likely cause of initial infection
 - Then spread by feces (?)
- Large refuse ponds, mosquito breeding sites
- NO threat to public
 - Heating kills virus in meat
- Threat to workers?
 - Turkey farmers
 - Skinning process



2004



West Nile Neuro-Invasive Disease Louisiana, 2004

[illegible]

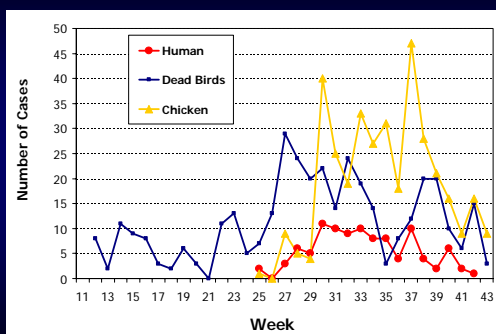
Louisiana Arboviral Surveillance, 2004

- Over 7,860 birds reported
- 1,215 birds tested and 582 WN+
- 208 Sentinel chicken conversions
- 937 Mosquito pools
- 49 Horses
- 101 Human cases
 - (75 NID, 22 Fever, 4 Asymptomatic)
- 7 deaths

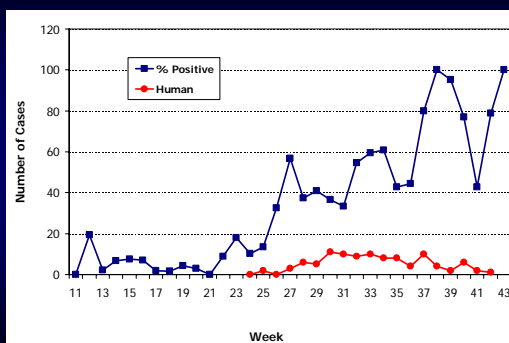
Louisiana Human Surveillance

- Serum and CSF are tested for antibodies
 - WN, St. Louis, LaCrosse, EEE viruses
 - Over 2,000/ year at State Lab
- People are no longer viremic by onset of symptoms
- Cross-reactivity
- Usually dx 2-3 wks post-onset
- 100-block address information provided to districts – pt confidentiality

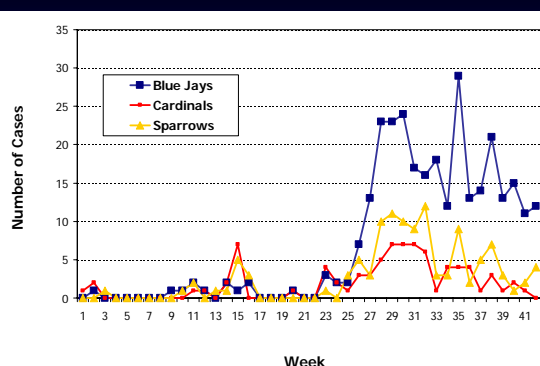
Counts of Humans & Birds



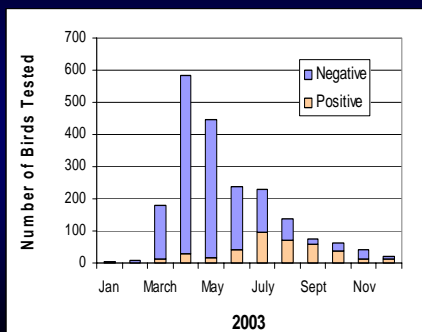
Human Case Count & Birds % Positive



WNV Positive Bird Species by Week



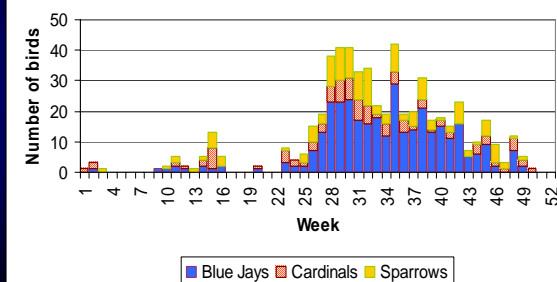
Number Positive of All Birds Tested by Month, 2004



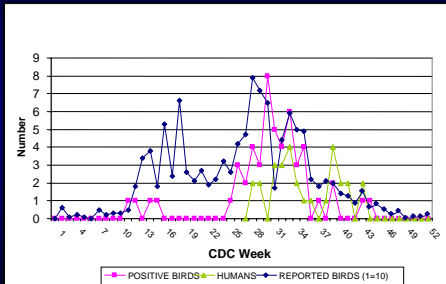
2004 Tested Dead Birds

Bird Type	No. Tested	No. Pos.	% Pos.
Blue Jay	504	337	66.9
Crow	78	45	57.7
Sparrow	330	139	42.1
Other	38	16	42.1
Cardinal	276	98	35.5
Raptor	51	18	35.3
Grackle	56	19	33.9
Seagull	6	2	33.3

2004 WNV Positive Birds by Species



Human Cases & Bird Surveillance EBR 2004

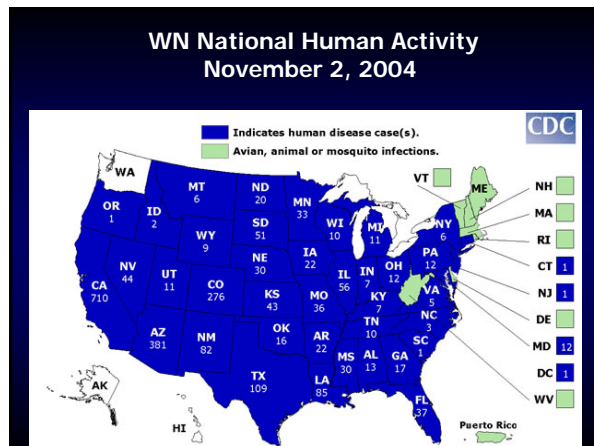


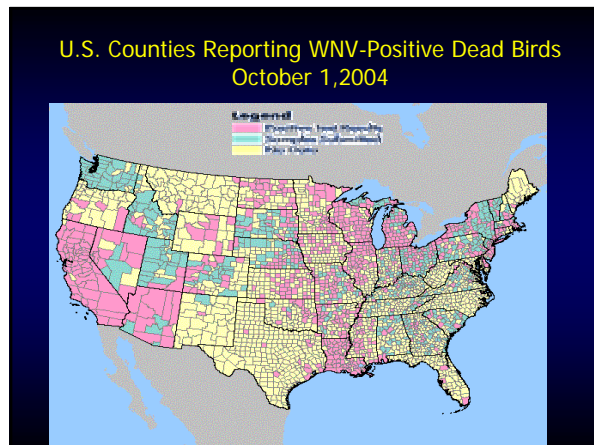
Interpreting WNV Surveillance Data

- Bird testing occurs year-round
- Detection dependant on public reporting
- A positive bird indicates that the virus is present (PCR)
- A number of positive birds from the same area, combined with active mosquito populations = a warning that transmission to humans can occur (usually 2 weeks)

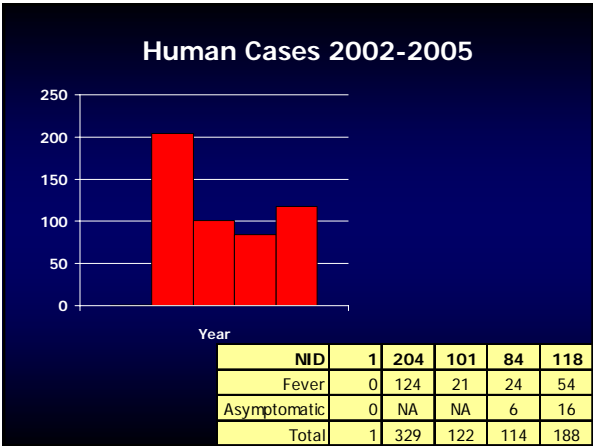
Bird Surveillance

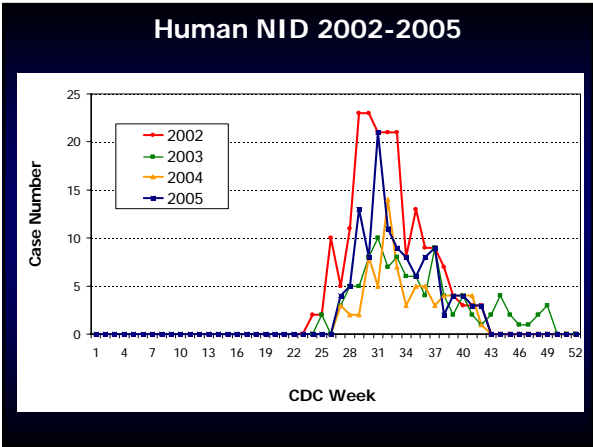
- Will most likely continue year-round
- Species tested will stay the same
 - Blue jay are probably most important
- Public participation?
- Best information as early warning
- Will improve LA ArboNet to give real-time information





Yearly Comparison



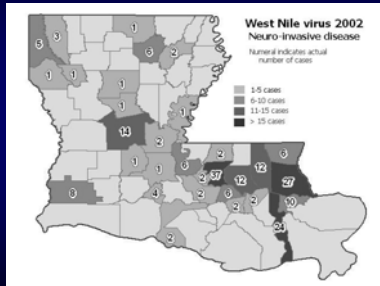


Birds /Mosquitoes, 2002-2005

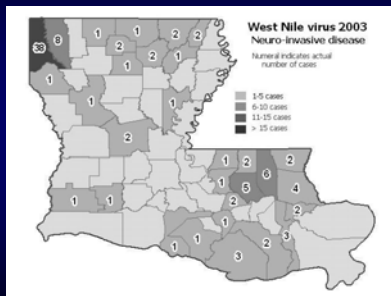
	2002	2003	2004	2005
Birds Reported	16,570	15,883	8,317	4,041 *
Birds tested	741	2,059	1,338	785
Birds positive	352	390	675	290
Blue Jays	332	189	338	165
Crows	16	36	44	16
Sparrow		81	138	62
Cardinal		62	97	34
% positive	47	19	50	37
Mosquito pool positive	238	201	988	1,441
C. quinque pos	206	137	820	1,400
Chicken seroconversions	451	387	226	177
Horse cases	362	36	62	16

* Reporting Terminated -8/29/2005

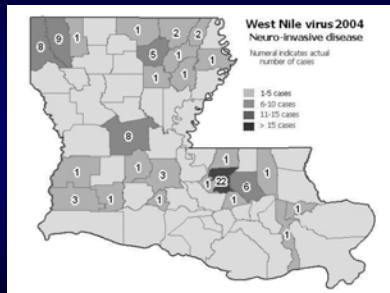
WNV NID, 2002

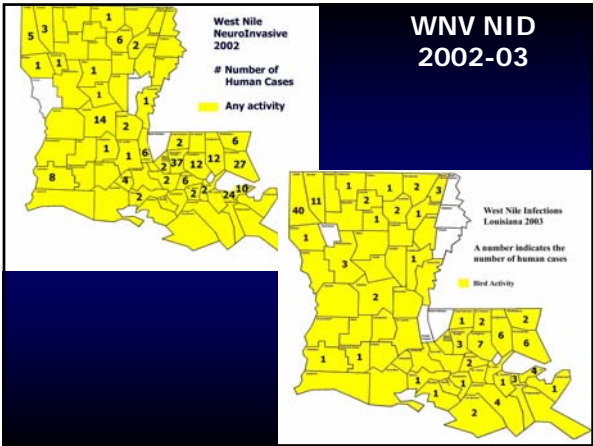


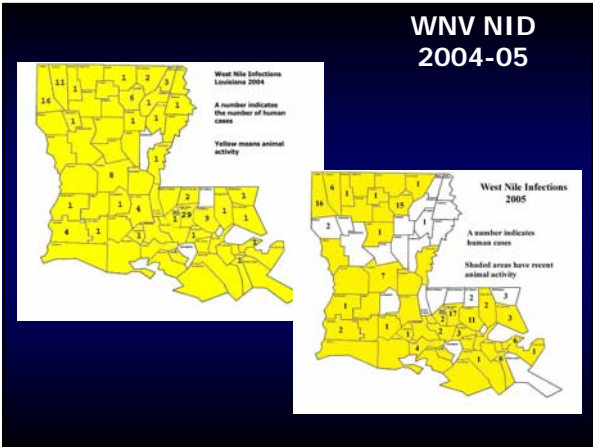
WNV NID, 2003



WNV NID, 2004









Environmental Inspection Results

- 2003 Human Cases – conducted in Shreveport/ Bossier city area (49% of total cases)
- Homes diverse in size, neighborhood type
 - **Most had outdoor seating
- Few had any standing water on property
 - **Most properties bordered an abandon home, vacant lot, or undeveloped property
 - **Most were within a block of a public drainage canal, all of which had standing water

Canals (Bayous)



Clutter, Containers, Overgrowth & Abandon Property



Exposure Factors

- Usually assume cases most likely infected in or around home
- 2002 – many cases older, retired, unemployed or disabled – no occupation reported
- 2003 follow-up investigation
- 67 cases contacted by phone
- 60% of those with occupations (58) reported outdoor occupations
- 60% were outdoors at dusk for 2 hrs or more activities included: sitting 80%, walking 82%, gardening 58%

Risk Factors

WNV and Hunting?

- Males contacted were 3x more likely to develop encephalitis/ meningitis ($p < 0.05$)
- 39/67 males – 87% hunters
- 45-60 yr old age group, elevated risk NID
- 67% hunt deer
- 47% woods, 24% marsh, 29% both
 - Marsh - 60% fresh, 40% salt
- Hunting locations most often reported Caddo, St. Tammany and Bossier
- 85% hunters did not report wearing repellent


Household Characteristics

- Some cases reported rarely leaving the home (2002)
- Breeding sites around home -
 - 61% flower pots, 33% bird baths, 40% other containers that hold untreated water
 - Within 1 mi of property: 69% canal/ ditch, 52% water body (lake), 38% wooded area
- 60% reported treatment by public control
 - 28% did own pest control for mosquitoes



NIOSH Recommendations for Outdoor Workers

- Make insect repellants available
- Recommend workers wear long-sleeves, long pants and socks when possible
- Eliminate sources of standing water
 - Remove trash like discarded tires
 - Turn over, cover or remove containers that accumulate water
 - Clean out gutters and ditches

Prevention




Preventing Arboviral Encephalitis in Louisiana



We all must work together to prevent encephalitis

Most arboviral encephalitis are mainly an infection of birds transmitted from bird to bird by mosquitoes. Occasionally a mosquito carrying the encephalitis virus bites a person.



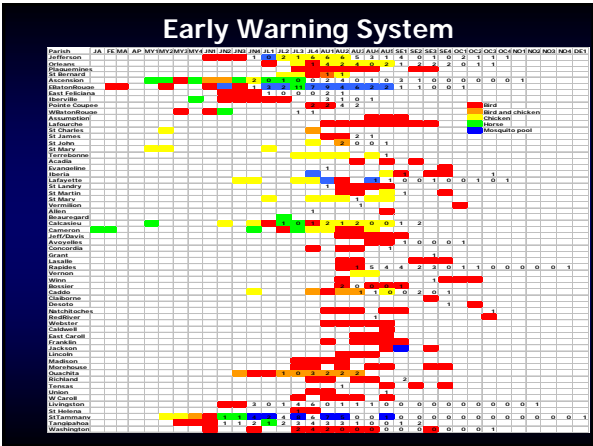
Prevention Overview

Prevention consists of:

- 1-An early warning system to detect the presence of virus in an area
- 2-Reduction of the numbers of mosquitoes
 - by destroying mosquito larvae in standing water
 - by killing adult mosquitoes before they bite people
- 4-Prevent mosquitoes from biting people
- 5-Diagnose encephalitis early to minimize the consequences of the disease

Early Warning System


- People collect and report dead birds: particularly crows, blue jays and birds of prey
- Local mosquito control traps mosquitoes
- Public health transport specimens
- LSU Veterinary labs tests birds and mosquitoes
- Public Health keeps track of results of birds and mosquitoes and warns mosquito control and the public



Can Chickens be Used as Sentinels?

- Highly susceptible (for development of antibodies)
- Resistant to mortality
- Non-infectious to each other
- Non-infectious to handlers
- Non-infectious to mosquitoes

- Chicken flocks established at known transmission foci
- Birds are bled periodically
- Serum samples sent immediately for testing
- HI or M-ELISA test used for screen
- N test for confirmation (3 days)
- Positives replaced for accurate monitoring





Surveillance

- Dead birds (especially crows)
- Mosquitoes
- Live wild bird sentinels
- Live captive sentinels (e.g. chickens)
- Veterinary surveillance
- Human surveillance

Encephalitis Tracking by the Infectious Disease Section

- Disseminates information via the Health Alert Network
- Communicates with the Centers for Disease Control and participates in the national "Arbonet" surveillance system
- Communicates with the Department of Agriculture, the LSU Veterinary laboratory and the veterinarian community
- Collaborates with Tulane University to update information on Arbonet, a repository of data on all encephalitis in Louisiana available through website
<http://arbonet.caeph.tulane.edu>

Encephalitis Tracking by the Infectious Disease Section

- Tracks all cases of encephalitis in people, birds, horses and mosquito
- Analyzes data, studies trends, communicates with local mosquito control, regional and parish health unit staff, hospitals and private physicians
- Provides consultation to physicians regarding diagnosis of arboviral encephalitis
- Provide medical and epidemiologic expertise during outbreaks
- Develops guidelines for surveillance
- Evaluates the encephalitis situation to make recommendations for the development of a comprehensive encephalitis control program for the whole state

Diagnosis by the Office of Public Health Laboratory

- Provides free of charge laboratory tests on blood and spinal to detect virus and antibodies to all types of arboviral encephalitis in Louisiana
- Rapid results
- Positive results communicated to the public and local mosquito controls to allow rapid implementation of preventive measures
- Participation in CDC quality control programs

Early Diagnosis in People

- People need to know the early signs of encephalitis: Fever and brain troubles (confused, disoriented, comatose, difficulty seeing, hearing, speaking must be checked quickly)
- The public health laboratory provides a rapid free diagnosis for cases with brain involvement

Mosquito Control

- Efficacy of control mechanisms?
 - Source reduction
 - Larvicide
 - Adulticide – routine and emergency intervention
- Resistance baseline data and resistance management practices?



Center of Environmental Health Entomologist

- Reviews mosquito control plans
- Provides consultation to mosquito control programs
- Provide entomologic expertise during outbreak

Reduce the Numbers of Mosquitoes

- People should get rid of standing water around their house; most of the mosquitoes that bite you are from your neighborhood
- Local mosquito control kills larvae from large areas of standing water. This is very effective before viruses are transmitted to people
- Local mosquito control kills adult mosquitoes spraying from trucks, plane or even going house to house in special occasions

Promotion of Mosquito Control Activities

- Provide risk assessment and consultation to local government on mosquito control programs

Health Education

•Advice on encephalitis prevention communicated through press releases, radio and TV interviews, website and pamphlets

<http://www.dhh.louisiana.gov/offices/?id=249>

•Collaboration with local community groups to promote health education and behavior modification

•Educational programs for medical professionals, satellite conferences, lectures

Promotion of Mosquito Control Activities

•Provide risk assessment and consultation to local government on mosquito control programs

Prevent mosquitoes from biting people

•Public health and the media let you know where the arbovirus are threatening people

•People can prevent mosquitoes bites

•Mosquitoes are NOT welcome in your home. The most dangerous mosquitoes bite late at night when you are sleeping. Make sure mosquitoes cannot enter your house. Doors or windows should be closed or have screens in good condition.

•When you are out - wear long sleeve shirts and long pants and avoid dark colors which attract mosquitoes.

• Apply insect repellent

FightTheBite Campaign

